REMARKS

Claims 1-5, 23 and 31 have been amended

Claims 1-5, 23 and 31 have been amended by adding the adjective "synergistically" to the term "effective amount". Support for this amendment is found in the original specification as filed. For example, the specification describes greater-than-additive effects for the co-administration of a chromium complex and biotin on pages 15 and 25 of the specification.

Claims 1-20 and 23-27 are not obvious under 35 U.S.C. §103(a)

Claims 1-37 were rejected in the first Office Action as being unpatentable under 35 U.S.C. §103(a) over McCarty (U.S. Patent Nos. 5,789,401 or 5,929,066), in view of de la Harpe et al. (U.S. Pat. No. 5,948,772) and Brand-Miller. Applicant argued against these rejections in the response to the first Office Action, but the Examiner was not persuaded. Claims 1-20 and 23-27 remain rejected in the present Office Action.

In order to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success provided by the prior art and/or generally available knowledge. Finally, the prior art references must teach or suggest all the claim limitations. M.P.E.P. §2143.

The Examiner asserts that the prior art discloses sufficient information that one with skill in the art would have been motivated to create and use the claimed invention. To support this assertion, the Examiner claims that the de la Harpe reference discloses a direct relationship between defects in carbohydrate metabolism in diabetics and hyperlipidemia. Specifically, the Examiner states that "due to ineffective insulin and compromised glucose metabolism *in diabetics*, the body must rely on lipid metabolism to meet its energy requirements resulting in hypercholesterolemia" (page 3 of Paper No. 7, emphasis added). Applicant respectfully disagrees. The Examiner claims that the cited passage in the de la Harpe reference refers to *diabetic* individuals, but it does not. The passage referred to by the Examiner in the de la Harpe reference discusses the conclusions of studies of *diets deficient in chromium*:

> "*Chromium depletion* results in biologically ineffective insulin and compromised glucose metabolism. *Under these conditions*, the body must rely primarily on

lipid metabolism to meet its energy requirements, resulting in the production of excessive amount of acetyl-CoA and ketone bodies." (de la Harpe et al., column 1, lines 26-31, emphasis added)

There is no indication that any of the individuals or animals in the studies that provided the data for the statements in the text were suffering from diabetes or any pre-diabetic condition. The information and conclusions from the cited passage refer to an artificial condition of chromium depletion. Thus the effects described in de la Harpe et al. are ascribed to and caused by chromic depletion, not diabetes. The Examiner indicates that the McCarty references state that biotin supplementation is useful in treating the glucose intolerance of type II diabetes. The McCarty references do not disclose, however, that biotin supplementation has any effect on the lipid profile of normal or diabetic individuals. While the disclosures of the prior art link chromium supplementation with the alleviation of a range of diabetic conditions, it cannot be assumed that an entirely different compound that is useful for treating one of the conditions associated with diabetes would automatically have any utility in the treatment of another condition associated with diabetes. It would have been clear to one with skill in the art that impaired glucose metabolism and other conditions associated with diabetes can have many causes and contributing factors, of which chromic depletion would be just one. It would also have been clear that while hypercholesterolemia and other forms of dyslipidemia are associated with diabetes, all forms of dyslipidemia can occur without diabetes or pre-diabetes syndromes being present, including impaired glucose metabolism and insulin insensitivity. From the information provided in the prior art, one with skill in the art would not be able to conclude with a reasonable expectation of success that biotin supplementation would help with the treatment of any form of dyslipidemia, alone or in combination with a chromium complex. In order to establish the utility of biotin treatments for diabetic conditions other than improper glucose metabolism, experimentation would have been necessary. Thus the combined disclosures of the referenced prior art documents do not provide a clear and reasonable link between biotin supplementation and the treatment of dyslipidemia.

The present invention is based on the surprising discovery of the synergy of biotin and chromium complex co-administration on insulin activity, glucose metabolism, hypercholesterolemia and dyslipidemia. The greater-than-additive effects of the co-

administration of biotin and chromium are described in the specification and illustrated in the data provided in the figures. To emphasize the synergistic nature of the co-administration effect, the term "synergistically" has been added to Claims 1-5, 23 and 31.

With regards to the use of chromium and biotin to specifically target post-prandial hyperglycemia, the Examiner asserts that the Applicant has only "recognized another advantage which would flow naturally from following the suggestion of the prior art" and that the differences between the present invention and the prior art are obvious. However, the claims have now been amended to emphasize the synergistic effects and benefits of the co-administration of chromium complexes and biotin in the treatment of dyslipidemia and post-prandial hyperglycemia and for the lowering of the glycemic index (GI) of a food. For example, the synergistic effects and benefits of the co-administration of chromium complexes can be seen in the data presented in Figure 2 for glucose metabolism and Figure 14 for changes in levels of HDL ("good") cholesterol, in addition to the discussion on pages 15 and 25. There is no disclosure or suggestion in the prior art that would lead one with skill in the art to believe that the co-administration of chromium and biotin would create anything but an additive effect. Additionally, with no suggestion of a synergistic effect, the prior art cannot teach or suggest the limitation of the claims to a synergistically effective amount.

As for pending claims directed toward the lowering of the GI of a food, the Examiner asserts that since the prior art discloses the use of chromium and biotin to treat diabetes, it would have been obvious to one with skill in the art to add chromium and biotin to food, with the expectation that a diabetic's blood glucose profile would be normalized by eating the food. The claims have now been amended to specify a *synergistically* effective amount of the compounds. The prior art lacks any data or discussion that discloses or suggests the existence of the *synergistic* effects of co-administering a chromium complex and biotin simultaneously.

The prior art does not disclose the treatment of dyslipidemia with biotin, nor does it provide data to support the use of biotin to treat dyslipidemia without undue experimentation. The prior art also does not contain any data or discussion to suggest that results and conclusions drawn from studies of the effects of chromium supplementation or chromium depletion on conditions associated with diabetes can be automatically applied to other compounds. While the prior art discloses that chromium supplementation or depletion can affect multiple conditions associated with diabetes, no scientific evidence is provided of any interrelationship between

those multiple conditions, such as a cause and effect-type relationship. Therefore, one with skill in the art, given the disclosure of the prior art, would not be able to assume that supplementation with biotin would be able to ameliorate any other condition associated with diabetes besides the disclosed benefits on blood glucose levels. There is no suggestion or motivation provided by the prior art to use *synergistically* effective amounts of biotin and chromium complexes for the treatment of dyslipidemia or for lowering the GI of a food. Without disclosing the synergistic effects of biotin and chromium co-administration or linking biotin supplementation directly to beneficial effects on serum lipid levels, the prior art cannot provide a reasonable expectation of success and certainly does not teach or suggest all of the limitations of the present claims. Applicants respectfully request the rescission of the claim rejections made under 35 U.S.C. §103(a).

CONCLUSION

Based on the arguments above, Applicants request the removal of all claim rejections and assert the application is ready for allowance. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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